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THE ACUTE MORTALITY RESPONSE OF BEAGLES TO MIXED GAMMA-NEUTRON RADIATIONS AND 250 KVP X RAYS

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FOREWORD
(Nontechnical summary)

Median lethality studies are conducted at the Armed Forces Radiobiology Research Institute (AFRRI) using a variety of mammalian species and radiation sources. In these studies, groups of animals are irradiated at selected doses throughout the lethal range (that range of doses resulting in deaths of 1 to 99 percent of the exposed animals[6] within 60 days).

If a large number of groups is irradiated over the entire lethal range, an "S" shaped response curve is produced when the percent of animals that die is plotted versus radiation dose. Only that portion of the curve between 10 and 90 percent response is generally linear. However, there is a mathematical transformation which changes the entire curve to a straight line. Such a line can be readily fitted to experimental data by a statistical method.

The surviving fraction of animals can be predicted for any dose by use of the response curve. The greater the number of animals involved and the nearer the dose to the 50 percent response point of the curve, the more accurate the prediction tends to be.

The LD_{50} dose is a frequently used parameter obtained from analysis of lethality data. It is that dose of radiation required to kill, within a specified period, 50 percent of the individuals in a large group of animals.

There are several applications for the information derived from this research at AFRRI. By comparing the results of median lethality studies in a variety of mammalian species, important trends or patterns may be discovered which could

aid in anticipating man's response to similar exposures. The LD_{50} and other characterizing features of the dose response curves are also used as base lines for evaluating response modifying factors such as protective agents, partial body shielding, changes in depth dose distribution, variations in dose rate, and combinations of injuries. In addition, new radiation sources can often be described from the standpoint of biological effects by median lethality studies.

The research reported herein provides dose response curves (Figure F-1) for beagles exposed to 250 kVp x rays and TRIGA reactor (mixed gamma-neutron) radiations delivered at 17 rads/min. The 60-day median lethal doses ($LD_{50/60}$) were calculated to be 206 ± 3.6 and 218 ± 3.0 rads (midline tissue) for the x rays and mixed gamma-neutron radiations, respectively. In addition, some clinical signs associated with acute radiation injury were followed in the study and are discussed.

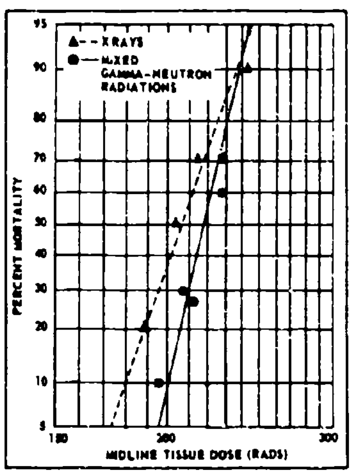

Figure F-1. Dose response curves

ABSTRACT

Beagle median lethality studies were conducted using 250 kVp x rays and TRIGA reactor (mixed gamma-neutron) radiations. Purebred beagles were irradiated at midline tissue doses from 166 to 292 rads. The dose rates were approximately 17 rads/min, and exposures were Class A uniform. $LD_{50/60}$ values of 206 ± 3.6 and 218 ± 3.0 rads were obtained for the x rays and the mixed gamma-neutron radiations, respectively. The RBE of the mixed gamma-neutron radiations was 0.94. Hematological values, clinical symptoms, and survival time data were also collected.

I. INTRODUCTION

Radiation lethality studies in mammals are an important portion of the research conducted at the Armed Forces Radiobiology Research Institute (AFRRI). An objective of these studies is to establish median lethality values (LD_{50}'s) in several species with respect to the radiation types, energies, and dose rates available at this laboratory. The LD_{50} end point is important in evaluating response modifying factors such as protective agents, sensitizing agents, changes in distribution of dose, variations in dose rate, and combined injuries.

The purebred beagle is the experimental animal of choice in a number of studies at the AFRRI because it is a well standardized and easily handled breed of dog, and because many hematological parameters of the dog are quite similar to those of man. The research herein reported was undertaken as an essential phase of portraying the beagle's response to ionizing radiations. It represents a further step in the orderly progression of median lethality data accumulation on mammals of various body sizes.

An LD_{50} value for beagles exposed uniformly to mixed gamma-neutron radiations at 17 rads/min was calculated from the data obtained in this study. In addition, the corresponding LD_{50} for 250 kVp x rays was determined for use as a comparison standard and as base line information for future research efforts.

Other laboratories have conducted similar studies. Ainsworth et al.[1] have recently reported an $LD_{50/30}$ midline tissue dose of 203 rads for mixed gamma-neutron radiations in mongrel dogs (40 rads/min, uniform exposure). The gamma/neutron ratio of the radiations used in their research differed significantly from that

available at this laboratory (0.19 vs 1.5) even though similar TRIGA reactors served as sources. Furthermore, differences in experimental animals, dosimetry techniques, exposure conditions, and the wide 95 percent confidence interval (183-219 rads) indicate their LD_{50} value would not be applicable to beagles exposed to the mixed gamma-neutron radiations at AFRRI without independent confirmation. Alpen et al.[2] and Bond et al.[5] have reported LD_{50} values for dogs with respect to 250 kVp x rays. However, differences again exist in animals, exposure conditions, and dosimetry techniques which necessitate an independent evaluation of that LD_{50} before it is used as a reference in other studies at AFRRI.

II. METHODS AND MATERIALS

Animals

The animals used in this study were healthy, purebred, AKC registrable beagles, 2 to 3 years of age and equally divided as to sex. They were bred and maintained in a closed colony at Richard E. Saunders, Inc., Richmond, Virginia. While at that facility, the dogs were immunized against distemper and rabies. At least 4 weeks prior to irradiation the dogs were transferred to temperature controlled animal rooms at the AFRRI. The dogs were then examined for parasite infestations, blood specimens were analyzed at least twice, and necessary veterinary care was provided. They were maintained individually in stainless steel cages (which were washed daily and sanitized weekly), fed kibbled laboratory dog food supplemented once a week with a high protein canned meat ration, and provided with fresh water ad libitum. During the 2 weeks immediately preceding exposure, animals received no medication nor were they subjected to any form of manipulation.

Radiation Exposures

A radial beam generator was used for the x irradiations. It was operated at a tube voltage of 250 kVp and a current of 30 mA. The total filtration of 0.95 mm Cu and 1.2 mm Be resulted in a half value layer of 1.9 mm Cu.

For the x-ray exposures, beagles were restrained in a Plexiglas* box and positioned in a circular arc about the x-ray generator as illustrated in Figures 1 and 2. Variation in the exposure rate throughout the center line of the box was less than 8 percent from the mean. The Pl[illegible]las box was adjustable in width and constructed to maintain the animal's center line normal to the primary x-ray beam minimizing any variation in the distance from x-ray source to beagle center line. Limited movement of the head was, however, possible. The box was secured to a turntable and

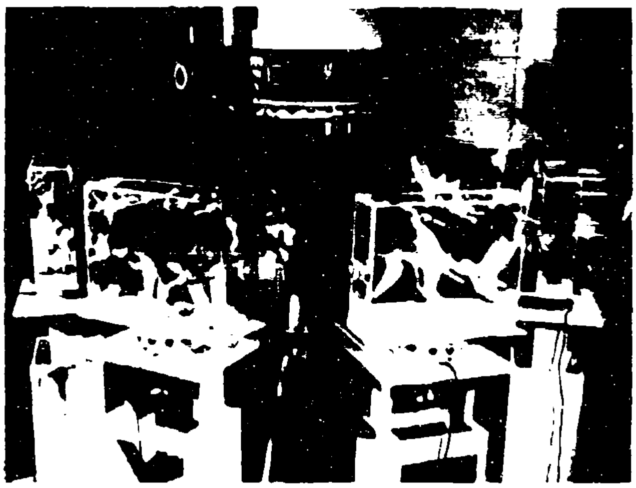

Figure 1. Animal array in x-ray exposure facility

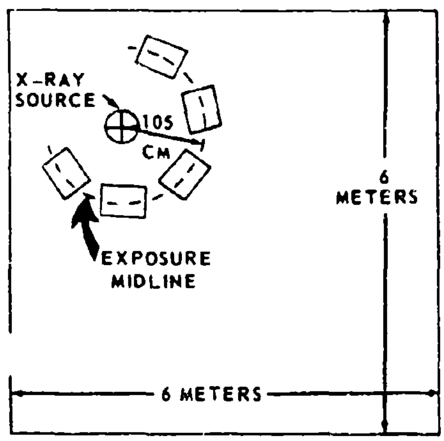

Figure 2. Plan view of x-ray facility

* Trade name for the transparent acrylic plastic manufactured by Rohm and Haas of Philadelphia, Pennsylvania.

midway through irradiation, animals were rotated 180° to provide bilateral exposure conditions.

The absorbed dose rate at the center of the animal was calculated from three factors. First the exposure rate, free-in-air, was determined at the position occupied by the center line of the animal. A Victoreen Rate Meter was used for these measurements. Second, the ratio of the exposure rate in a heterogeneous tissue equivalent beagle phantom to the exposure rate, free-in-air, was determined. Miniature tissue equivalent ionization chambers were used for these measurements. Third, the conversion factor, f, of 0.95 for muscle and for this quality of radiation was obtained from the International Commission on Radiological Units and Measurements (ICRU) Report 10b.[8] The product of these factors gave the absorbed dose rate at the center of the an nal. This dose rate was 16.8 rads/min.

The depth dose measurements indicated that the exposures were Class A, uniform as defined in ICRU Report 10e[9] (Figure 3).

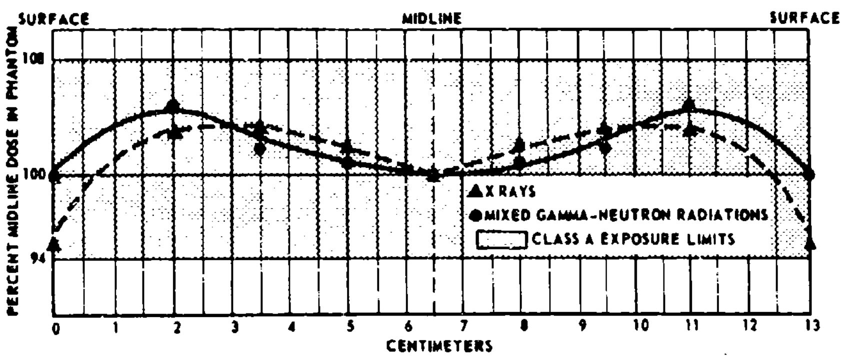

Figure 3. Dose profiles in beagle phantom (midchest level) bilaterally exposed to x rays and to mixed gamma-neutron radiations

Eighty-two animals were exposed, 4 or 5 at a time, to a total of 8 midline tissue doses. The doses ranged from 175 to 271 rads. In addition, 10 control animals were sham irradiated.

The AFRRI-TRIGA reactor and exposure facilities, described in detail elsewhere,[11] were used for the mixed gamma-neutron irradiations. Animals were positioned in an arc with their midline 292 cm from the reactor core center line, Figures 4 and 5. The same Plexiglas boxes, turntables, and bilateral exposure protocol of the x-ray studies were used for the mixed gamma-neutron irradiations.

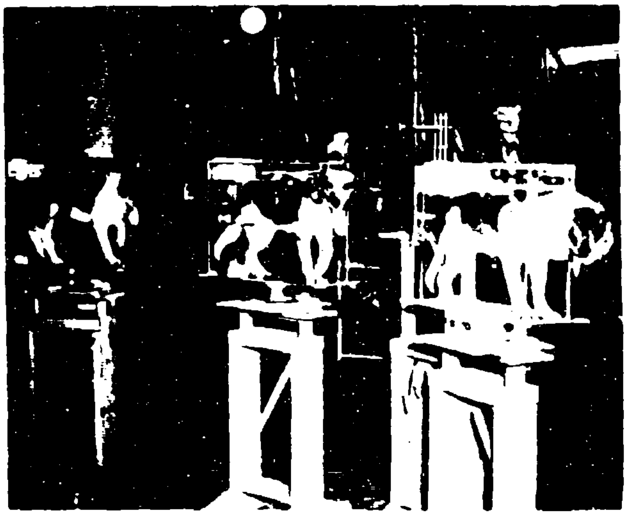

Figure 4. Animal array in reactor exposure room

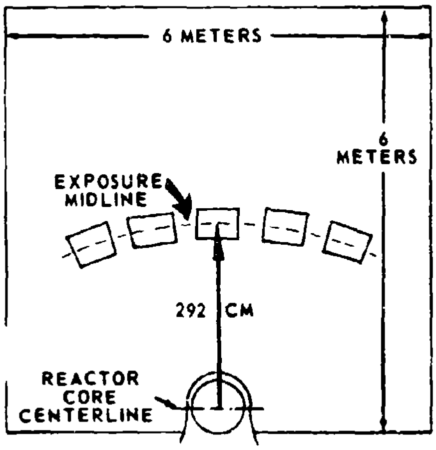

Figure 5. Plan view of reactor exposure room

The absorbed dose rate at the midline of the animal was calculated from two factors. First, the tissue kerma rate, free-in-air, was obtained from measurement with a 50 cm^3 cavity tissue equivalent plastic walled ionization chamber. Second, the ratio of the absorbed dose in the center of the beagle phantom to the tissue kerma, free-in-air, was obtained; miniature tissue equivalent ionization chambers were used

for these measurements. The product of these two quantities gave the absorbed dose rate at the center line of the animal.

Approximately 60 percent of the tissue kerma measured free-in-air was due to gamma radiations, 30 percent to neutrons with energies greater than 10 keV, and 10 percent to slower neutrons. The effective gamma energy was between 1 and 2 MeV.

A total of 83 animals was exposed in grouns of 4 or 5 at 10 midline tissue doses of mixed gamma-neutron radiation. Doses ranged from 166 to 292 rads. Twenty control animals were sham irradiated.

Depth dose measurements indicated that the gamma-neutron exposures were also Class A uniform (Figure 3). The distribution of dose from nose to tail along the midline of the phantom varied less than 5 percent from the mean.

Clinical Observations

Irradiated animals were checked at least once each 6-hour period during the experiment to determine the time of death, and particularly during the 1st day postexposure, to detect clinical signs of radiation injury. The observations were continued until all dogs in a group had died or until 60 days had elapsed since irradiation.

Three ml of blood for hematological examination were withdrawn from a jugular vein of all dogs two or more times prior to irradiation. Hematology base line values were established and the condition of the animals was monitored. After irradiation, blood specimens were collected at regular intervals from approximately one-third of the animals (2 males and [illegible] females from each dose group of 10 dogs), and hematological values were measured. Rectal temperatures were measured

whenever blood was obtained. Postmortem examinations were carried out on approximately half of the decedents with representative animals from each group in which deaths occurred.

III. RESULTS

Mortality Response

Beagle mortality data collected in this study are presented in Table I. The data were analyzed by digital computer using a modification of a United States Department of Agriculture program which computes a weighted linear regression line of the mortality probit response on the logarithm of the dose. The maximum

Table I. Beagle Mortality Data

Radiation type	Midline* Tissue Dose (rads)	Number of Animals in Group	Percent Mortality	Mean Survival Time (days)	Survival Time Range (days)
250 kVP x rays	271	4	100	13.5	12.75 - 14.75
	241	10	90	14.25	9.75 - 16.75
	237	4	100	15.25	14.75 - 16.25
	228	10	70	14.5	12 - 20
	215	10	70	15	13 - 17.25
	203	24	50	18	14.25 - 22.5
	189	10	20	15.5	14.75 - 16.25
	175	10	0	-	
Mixed gamma-neutron radiations	292	10	100	13.25	10.5 - 15.25
	284	4	100	12.75	10.5 - 15
	263	10	100	14.5	10 - 24
	235	10	100	16	12.5 - 19
	227	10	60	16	14 - 20.5
	215	4	0	-	
	211	11	27	15.5	13.75 - 16.5
	207	10	30	15.75	13.75 - 19.75
	195	10	10	15.5	15.5
	166	4	0	-	
SHAM (controls)		30	0		

* Roentgens of x rays measured at the midexposure volume were multiplied by 0.95 (rads in air/R) and by 0.95 (rads midphantom/rad in air) to obtain midline tissue dose.

Rads of mixed gamma-neutron radiations to a small tissue sample measured at the midexposure volume were multiplied by 0.81 (a factor arrived at in depth dose studies and calibration procedures) to obtain midline tissue dose

likelihood estimates of the essential parameters of a distribution as described by Finney[7] are thus obtained.

Lethality values and the corresponding 95 percent confidence limits from the analysis are shown in Table II.

Table II. Results of Beagle Mortality Data Analysis

Percent Mortality	Mixed gamma-neutron radiation		250 kVp x rays	
	Midline Tissue Dose (rads)	95% Confidence Limits	Midline Tissue Dose (rads)	95% Confidence Limits
10	200	186 - 207	180	162 - 189
30	211	202 - 216	195	184 - 202
50	218	212 - 225	206	198 - 214
70	226	220 - 238	218	210 - 230
90	238	230 - 259	236	225 - 260
Slope of regression line	33.6		21.6	

More than 95 percent of the deaths occurred during the period from 10 through 20 days postirradiation. Exceptions were: 1 dog died on day 9, 1 on day 21, 1 on day 23, and 1 on day 24. No difference in survival time was noted between corresponding x and gamma-neutron irradiated groups of animals. Mean survival times appeared to decrease slightly with increasing dose. However, ranges of survival times overlap for all dose groups (Figure 6) and no statistically significant dependence of survival time upon dose was detected.

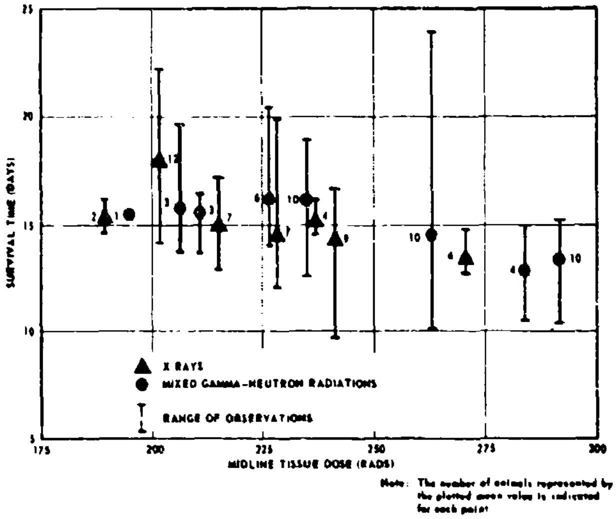

Figure 6. Beagle survival times

Vomiting

Vomiting has been a consistent clinical symptom in large mammal studies at this laboratory. In order to evaluate its usefulness as an indicator of radiation injury, the x-ray exposed animals and the last 40 dogs exposed to mixed gamma-neutron radiations were checked for vomiting at least hourly during the 1st day postirradiation.

From the information collected, no significant difference was detected in occurrence or frequency of vomiting between survivors and decedents considered in toto. The dose group in which all animals survived had the lowest (30 percent) vomiting incidence. Vomiting was noted in 50 to 90 percent of the dogs in dose groups where deaths occurred, but no dose dependent pattern was detected. Vomiting was seen in 60 percent of the animals that died later in the experiment.

Episodes of vomiting were seen throughout the 24-hour observation period; however, 30 percent of the episodes occurred between 2 and 4 hours postirradiation. In addition, approximately two-thirds of the animals that vomited had done so at least once within the first 4 hours after exposure.

Hematology

Blood specimens were taken from approximately one-third of the beagles after exposure to mixed gamma-neutron radiation (three times during the first week and once a week during the remainder of the experiment). It was important to determine if this procedure had a significant effect on survival of the animals. Therefore, the mortality data of the dogs from whom specimens were obtained were separately analyzed from the data from the unsampled dogs. The results are shown in Table III. The LD_{50}, LD_{10}, and LD_{90} values obtained were nearly identical in all cases and the confidence limits overlapped extensively. Similar results were obtained from the x irradiated dogs. In this latter case there were too few data for the programmed computer to calculate a significant regression line for the dogs from whom blood was

Table III. Comparison of LD_{50} Values for Mixed Gamma-Neutron Radiation in Dose Groups where Blood Specimens were Obtained from Some Animals Throughout the Experiment

	LD_{50} (rad)	95% Confidence Limits	Slope of regression line
All Beagles	217	210 - 224	33.4
Sampled* Beagles	217	205 - 230	34.4
Unsampled Beagles	216	207 - 227	32.4

*Sampling consisted of withdrawing 3 ml of blood from a jugular vein 3 times during the first week postirradiation, and once a week thereafter.

drawn. However, the calculations for the unsampled dog data agreed with the results from the pooled data.

A marked fall in white blood cell count was noted 1 day after irradiation for all dogs examined (lymphocytes averaged 25 percent of normal values and neutrophils approximately 75 percent). Minimum lymphocyte counts occurred either on day 1 or day 2 postexposure. Subsequently, lymphocyte counts increased slowly, and after 60 days, were still much less than preexposure values. The 2-week postexposure specimens contained the minimum number of neutrophils found. At 3 weeks postexposure the start of a rapid increase in circulating neutrophils was seen in survivors; however, preirradiation levels were not reached within the 60-day observation period. In the dose groups where all animals died, circulating neutrophils had essentially disappeared by the end of 2 weeks and lymphocytes were only 20 to 30 percent of normal values.

Neutrophil values remained higher in animals surviving an exposure than in those whose injury resulted in death. For example, in the 203-rad x-ray group where death occurred in 4 of 8 animals from whom postirradiation hematological values were obtained, minimums found for survivors averaged 965 cells/mm^3 (range: 500 to 1700). The corresponding minimum for the 4 decedents was 131 cells/mm^3 (range: 0 to 420).

Platelet counts were seen to fall rapidly after 1 week. Minimum values were found at 2 weeks postirradiation. Return to preirradiation levels was complete for all survivors within the 60-day experimental period. In dose groups where 100 percent mortality occurred, the last platelet counts prior to death were less than 1 percent of normal.

In the survivors, red blood cell (RBC) minimum counts occurred approximately 4 weeks postirradiation. Return to normal values was seen by the end of the 60-day observation period. In many of the survivors an increase in reticulocytes was noted after 4 or 5 weeks. In the 100 percent mortality groups the last RBC counts prior to death were about 65 percent of normal. Although the RBC count was depressed, in no case did it reach a level that would be representative of clinical anemia. The depression is most easily explained by normal attrition of the cells and a transient cessation of hemopoiesis.

Pathology

Approximately 60 percent of the decedents were weighed immediately after death. The average loss of preirradiation weight was 17 percent.

Hemorrhagic and infection associated lesions were the most prominent gross changes seen at necropsy. Hemorrhagic lesions, petechial and larger, were commonly found associated with many organs. Subepicardial hemorrhages were seen on the heart. Subendocardial hemorrhages were encountered routinely in the right atrium and less frequently in the other chambers of the heart. Subpleural hemorrhage, emphysema, and adhesions of the lungs were often evident. The gastric mucosa was generally hyperemic with occasional submucosal hemorrhagic lesions. Submucosal hemorrhages and occasional ulcers were seen in the small intestine. Extensive hemorrhage with ulceration and erosion was usually found in the colonic mucosa. The cortices of the kidneys were often congested; and occasional subcapsular hemorrhagic lesions were noted.

Rectal temperatures were measured in the control animals and in the dogs exposed to mixed gamma-neutron radiations from which blood specimens were obtained. All decedents had temperatures above 104°F prior to death. Less than half of the survivors exceeded this value, and the highest temperature recorded for control animals was 102.4°F.

IV. DISCUSSION

The LD_{50} obtained for 250 kVp x rays, 206 rads (midline tissue dose), is in good agreement with the 212 rads (midline tissue dose) quoted by Ainsworth et al.[1] for mongrel dogs. There is no statistical difference between these values at the 0.3 level. If the variation is real, it could be the result of their use of anesthesia during irradiation and/or the difference in dog strains used.

The 242 ± 4 rads (average absorbed dose) reported by Norris et al.[10] as the LD_{50} value for ^{60}Co gamma rays in bilaterally exposed purebred beagles is significantly different from our results for 250 kVp x rays at the 5 percent level of confidence. If their average absorbed dose is considered equivalent to the midline tissue dose used at this laboratory, the RBE of ^{60}Co gamma rays compared to 250 kVp x rays is 0.85 for median lethality in the beagle. This value is in agreement with that obtained by Sinclair[12] using a variety of end points.

The LD_{50} obtained for mixed gamma-neutron radiations of 218 rads differs from the LD_{50} for 250 kVp x rays at the 10 percent level of confidence. The RBE of AFRRI-TRIGA mixed gamma-neutron radiations is accordingly 0.94 for median lethality in the beagle. There is no significant difference between our results for

mixed gamma-neutron radiations and those of Ainsworth et al.[1] at the 5 percent level of confidence because of the overlap of their 95 percent confidence limits (183-219 rads) with those calculated for this study (212-225 rads).

Other research[13,14] at this laboratory, produced median lethality end point RBE values of 1.7 in rats and 1.3 in monkeys for the mixed gamma-neutron radiations. It thus appears the RBE of the mixed gamma-neutron radiations decreases as a function of body size. The 0.94 value is, therefore, not unreasonable. Furthermore, it is in agreement with the work of Bond et al.[5] and Alpen et al.[3] who also used mixed radiation fields (predominately neutrons) and found the RBE to be less than 1 for median lethality in dogs when 250 kVp x rays were used as the standard for comparison.

The slopes of the dose response curves indicate that response among individuals is less variable to mixed gamma-neutron radiations than to x rays. This effect has been noted in other animals at this laboratory[13,14] as well as by other investigators.[3,5]

In addition, the beagle response curves tend to have steeper slopes than those for mongrels.[1,2,3,5] That result agrees with Andrews'[4] observation that "A homogeneous population such as an inbred strain will have a narrower [lethal] dose range than is found for a more heterogeneous group."

Hemograms developed in this study appeared similar to those of Alpen et al.[2] particularly with respect to platelets and leukocytes. Changes noted at postmortem examination were not unique and have generally been reported.

V. CONCLUSIONS

The effects of whole body exposure to x rays and mixed gamma-neutron radiation in the young adult beagle were studied. The following conclusions were reached:

1. The beagle LD_{50} for 250 kVp x rays (1.9 mm Cu HVL) at 17 rads/min was 206 rads (midline tissue dose). The corresponding LD_{50} dose for mixed gamma-neutron radiations from the AFRRI-TRIGA reactor was 218 rads. The mixed gamma-neutron radiations, when compared to 250 kVp x rays, had an RBE of 0.94 for median lethality in the beagle.

2. Survival time of the decedents in this study was not a function of the type of radiation nor was it shown to be dose dependent over the lethal range.

3. Survival times, hematology studies, and changes seen at necropsy indicate that injury to the hematopoietic system was the primary cause of death in this investigation.

4. Vomiting was not dose dependent in the groups of dogs in which deaths occurred. However, a majority of the beagles irradiated at midtissue doses from 189 rads to 292 rads vomited. Vomiting occurred most frequently between 2 and 4 hours postexposure.

5. The collection of blood specimens from irradiated animals did not affect survival in this study.

6. Individual response to the mixed gamma-neutron radiations was less variable than was the response to x rays.

REFERENCES

1. Ainsworth, E. J., Leong, G. F., Kendall, K. and Alpen, E. L. Comparative lethality responses of neutron- and X-irradiated dogs: influence of dose rate and exposure aspect. Radiation Res. 26:32-43, 1965.

2. Alpen, E. L., Jones, D. M., Hechter, H. H. and Bond, V. P. The comparative biological response of dogs to 250-kvp and 100-kvp x-rays. Radiology 70:541-550, 1958.

3. Alpen, E. L., Shill, O. S. and Tochilin, E. The effects of total-body irradiation of dogs with simulated fission neutrons. Radiation Res. 12:237-250, 1960.

4. Andrews, H. L. Radiation Biophysics, Englewood Cliffs, N. J., Prentice Hall, Inc., 1961.

5. Bond, V. P., Carter, R. E., Robertson, J. S., Seymour, P. H. and Hechter, H. H. The effects of total-body fast neutron irradiation in dogs. Radiation Res. 4:139-153, 1956.

6. Cronkite, E. P. and Brecher, G. The protective effect of granulocytes in radiation injury. Ann. N. Y. Acad. Sci. 59:815-833, 1955.

7. Finney, D. J. Probit Analysis, 2nd Ed. Cambridge, England, Cambridge University Press, 1952.

8. International Commission on Radiological Units and Measurements (ICRU) Report 10b, 1962. Physical aspects of irradiation. National Bureau of Standards Handbook No. 85. Washington, D. C., U. S. Government Printing Office, 1964.

9. International Commission on Radiological Units and Measurements (ICRU) Report 10e, 1962. Radiobiological dosimetry. National Bureau of Standards Handbook No. 88. Washington, D. C., U. S. Government Printing Office, 1963.

10. Norris, W. P., Rehfeld, C. E., Poole, C. M. and Williamson, F. S. Mortality in beagle dogs following a single dose of Co^{60} gamma-radiation. Argonne, Illinois, Argonne National Laboratory Annual Report ANL-7136, pp. 113-115, 1965.

11. Seigneur, L. J. and Brennan, J. T. Incapacitation in the monkey (Macaca mulatta) following exposure to a pulse of reactor radiations. Bethesda, Maryland, Armed Forces Radiobiology Research Institute Scientific Report SR66-2, 1966.

12. Sinclair, W. K. The relative biological effectiveness of 22-Mevp X-rays, cobalt-60 gamma rays, and 200 kvcp X-rays. VII. Summary of studies for five criteria of effect. Radiation Res. 16:394-398, 1962.

13. Stanley, R. E., Seigneur, L. J. and Strike, T. A. The acute mortality response of monkeys (Macaca mulatta) to mixed gamma-neutron radiations and 250 kVp x rays. Bethesda, Maryland, Armed Forces Radiobiology Research Institute Special Publication SP66-23, 1966.

14. Strike, T. A., Seigneur, L. J. and Stanley, R. E. Acute mortality of mice and rats exposed to mixed gamma-neutron radiations or to x rays. Bethesda, Maryland, Armed Forces Radiobiology Research Institute Scientific Report SR68-6, 1968 (in press).

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13 ABSTRACT

Beagle median lethality studies were conducted using 250 kVp x rays and TRIGA reactor (mixed gamma-neutron) radiations. Purebred beagles were irradiated at midline tissue doses from 166 to 292 rads. The dose rates were approximately 17 rads/min, and exposures were Class A uniform. $LD_{50/60}$ values of 206 ± 3.6 and 218 ± 3.0 rads were obtained for the x rays and the mixed gamma-neutron radiations, respectively. The RBE of the mixed gamma-neutron radiations was 0.94. Hematological values, clinical symptoms, and survival time data were also collected.

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